AN ATTEMPT TO ANSWER THE QUESTION:

WHICH PART

OF THE PLANT

CONIUM MACULATUM

IS THE BEST FOR

MEDICINAL USE?

BY WM. MANLIUS SMITH,

MANLIUS, N. Y.

Reprinted from the Transactions of the N. Y. State Medical Society for 1867.

ALBANY:

VAN BENTHUYSEN & SONS' STEAM PRINTING HOUSE

1867.

If we place any confidence in the maxim, "*Ubi virus, ibi virtus*," we should expect to find in Conium maculatum a valuable medicinal agent; for, since the days of Socrates, it has been known that the hemlock in efficient quantities is capable of destroying life. But if we are to judge of its value by the degree of use commonly made of it by medical men, we can assign it only an inferior rank in the materia medica.

If we reflect, however, that the disuse into which Conium has fallen may have arisen from the circumstance that the preparations of it attainable by physicians, vary more in quality than those of most other medicinal substances, and that frequently these preparations are totally destitute of activity, we may think it worth our while to enquire if there is not some means by which such a degree of uniformity and stability can be given them as to render them worthy of the confidence and reliance of the medical profession.

It was with a view of fixing upon some good plan for securing this result, and also with the hope of adding, perhaps, something to the general stock of knowledge with regard to the therapeutic uses of the article, that the subject of Conium was accepted by the writer for examination. In the outset of the investigation, the fact presented itself that pharmacopœias differ as to the part of the plant recommended for medicinal use, the U. S. pharmacopœia directing the leaves, and the British the fruits or seeds. From all that could be gathered from the ordinary treatises on materia medica, it would seem that the seeds are the most active, but how much more energetic is not specified.

The first thing in order, then, seemed to be to settle by some precise and accurate experiments the difference, if any, existing in different parts of the plant as respects their activity. As the medicinal efficacy of Conium is believed to reside in the alkaloid, or alkaloids existing in it, the method of ascertaining the comparative quantities of these alkaloids that are contained in different

parts of the plant, presented itself as an available one for the purpose in view.

The plan adopted has been to make, as nearly as possible, precisely similar preparations from the leaves collected at two different stages of growth, and from the seeds at different degrees of maturity, and then by a delicate re-agent to test their comparative richness in the alkaloids. The re-agent used was that recommended by F. F. Mayer, in the Am. Journal of Pharmacy, vol. xxxv, p. 23, consisting of a dilute solution of iodide of potassium and corrosive sublimate in water. As comparative results only were aimed at, the following modification of the course of proceeding prescribed by Mayer was adopted: The various solutions to be tested were each diluted with carefully ascertained amounts of water, till but a faintly perceptible turbidity was produced on the addition of the test liquid, and the comparative strengths estimated by the amount of dilution that each solution admitted of.

The 30th of July, 1866, a quantity of leaves was collected from a Conium plant just fairly in flower. All withered and sickly looking portions, as well as the greater part of the petioles, both general and partial, having been rejected, four parcels of 500 grains each were accurately weighed out, and designated A^1, A^2, A^3 and A^4. Of these, A^3 and A^4 were each thoroughly bruised in a mortar for five minutes, and then transferred to a half pint bottle, and 1,000 grains, by weight, of diluted alcohol added. The mortar was well cleansed and dried between each operation. Parcels A^1 and A^2 were placed to dry, thinly spread out on paper, in a darkened room, and occasionally turned. The bottles containing A^3 and A^4 were well stopped with corks, covered with thick paper and placed in a cellar.

The same day, the leaves were collected from other plants wholly out of flower, and having the fruits on the more mature umbels nearly, if not quite, full grown. These leaves, the same care being used to reject inferior portions, were likewise weighed into parcels of 500 grains each, and designated B^1, B^2, B^3 and B^4, and were treated exactly as the corresponding parcels designated A.

The fruits that appeared to be full grown were collected from the same plants, that furnished the leaves designated B, by cutting off with scissors the umbellules entire. Four parcels of 500 grains each were made of them, designated C^1, C^2, C^3 and C^4, which were treated as parcels A and B had been.

The partly grown fruits from the same plants furnishing B and

C, consisting of those which had but just dropped the flower, and those that were about half grown, situated, as they were, on the same umbellules, were collected, by cutting off the umbellules entire, and four parcels of 500 grains each made and treated as before. They were designated D^1, D^2, D^3 and D^4.

On the 3d of August those parcels that had been placed to dry were weighed, and on the 23d of August were weighed again. The weights being essentially the same in both instances, it was concluded that the drying process had reached its limit. The several parcels weighed as follows: A^1 113 grains, A^2 110 grains, B^1 158 grains, B^2 159 grains, C^1 and C^2 each 183 grains, D^1 185¼ grains and D^2 183 grains.

A^2 (that is, the dried leaves from the plant in full flower), was pounded in a mortar till the powder all passed through a sieve of 37 meshes to the linear inch. In this operation it lost four grains. The remaining 106 grains was placed in a half pint bottle, and 390 grains of water and 1,000 grains of diluted alcohol added. The object of adding the water was to make the menstruum used, in effect, the same as that in which A^3 and A^4 had been put to macerate. Parcel A^1 was wrapped up, first in writing paper and then in thick brown paper, and laid on a shelf, for examination after a time sufficiently long to test its keeping properties.

B^2, or the leaves from the plants wholly out of flower, were treated in the same way that A^2 had been, except that 341 grains of water only, were needed to supply that lost in the drying process. Parcel B^1 was treated as A^1, as were also C^1 and D^1. C^2, or the full grown but unripe and green fruits or seeds, was powdered till 160 grains passed through the sieve. The remainder, consisting mainly of pedicels, weighed 20 grains. Both the 160 grains of powder and the 20 grains of pedicels were placed in a half pint bottle, and 320 grains of water and 1,000 grains of diluted alcohol added. D^2, or the full grown seeds, gave a weight in powder and pedicels of 177½ grains, and was treated with 320 grains of water and 1,000 grains of diluted alcohol. All the bottles, as before, were wrapped in brown paper and placed in the cellar. There they remained till January 18, 1867, when tinctures were made from each lot by percolation; a funnel, with the throat so obstructed with flax, as to deliver a drop about once a minute, being used as a percolator. A^3 was first placed in the funnel, and diluted alcohol poured on till a little over four ounces of liquid had passed, that is, till the four ounce vial used as a receiver was filled to a mark

on its neck. The tincture obtained was then transferred to the bottle in which the leaves had macerated, it having been thoroughly washed and dried—the exhausted matter removed from the funnel—the funnel well rinsed and wiped, and half an ounce of diluted alcohol passed through to rinse out the obstructing plug, before B^3 was introduced. In like manner B^3, C^3, D^3 and A^2, B^2, C^2 and D^2 were treated, the funnel being carefully cleansed between the percolations of the several parcels. The same amount of tincture was thus obtained from each, made as nearly as possible, with the same menstruum.

In order to apply the re-agent selected, it was next necessary to get rid of the alcohol in the specimens to be tested. A certain definite and equal portion of each (20 cubic centimetres, or between 5 and 6 fluid drachms), was taken, the same amount of a watery solution of oxalic acid added to each portion of tincture taken. which was then evaporated by a gentle heat, not rising above 110 deg. F, to approaching dryness. The residues were then diluted with water to the original volume of 20 c. c. each, and afterwards still further diluted, as occasion required, till they each were affected to the same faint degree of turbidity, by the application of the test liquid. It was found that the liquid from the leaves of the plant, just in full flower, admitted of a dilution with $1\frac{1}{2}$ times its volume of water. That from the leaves from the plant gone to seed, bore but $\frac{1}{4}$ its volume of water; that from the full grown seeds required dilution with 7 volumes of water, and that from the immature seeds gave a perceptible turbidity with the test liquid when diluted with 8 times its volume of water, making the comparative strengths, in the active principle, as follows: $A^3=10$, $B^3=5$; $C^3=32$, and $D^3=36$. These experiments showed the partly grown fruits to be the most active portion of the plant. The tinctures made from the several parcels of leaves and seeds after drying, gave very unexpectedly the same figures, with the corresponding tinctures made from the undried specimens; from which result the inference was drawn that the method of drying adopted, had not dissipated any of the active principle.

Some full grown fruits, collected in August 1859, dried in a darkened room and kept in a paper package on a shelf, exposed to the ordinary changes of temperature, from changes in the seasons, were also examined. A quantity of them were powdered till they passed through the sieve, of 37 meshes to the inch, and 177 grains of the powder, corresponding with the amount of pow-

der of seeds used in the previous experiments taken, moistened with water acidulated with oxalic acid, placed in a conical percolator, and water poured on till the same amount of liquid was obtained, as in the previous experiments. This solution was found to bear dilution with 7 volumes of water before reaching the limit of perceptible reaction with the test liquid. This seems to indicate that the dried seeds retain their activity unimpaired for upwards of seven years. But it should be borne in mind that as the summers of 1859 and 1866 probably differed in temperature, so the plants grown in those years may have differed in their original content of the active alkaloids.

Specimens of Fluid Extract of Conium, (U. S. P.), (that is, of dried leaves), prepared by Dr. E. R. Squibb, and also of Fluid Extract of Conium Seed, prepared by the same hands from the dried, full grown, but green fruits, were also tested in the way narrated above, the same amounts, 20 c. c. being operated on. The results obtained were, that the oxalic solution prepared from the fluid extract of the leaves bore dilution with 32 volumes of water, while that from the fluid extract of the seed bore dilution with 224 volumes of water, making the seeds in this case seven times as strong as the leaves.

It may be a matter of interest to state further, that a Fluid Extract of Conium bearing the label of Tilden & Co., and one with the label of Henry Thayer & Co., were also tested in the same manner. By this method the solution from Tilden's extract bore dilution with but $2\frac{1}{2}$ volumes of water, while that from Thayer's gave no reaction, even when undiluted. Some further investigation showed that this want of reaction was due, perhaps, to the presence of acetic acid, and so a modified form of the operation was tried with the three fluid extracts, i. e., Squibb's, Tilden's and Thayer's. The oxalic solutions obtained from 20 c. c. of the fluid extracts, were treated with solution of caustic soda till they gave decided alkaline reactions. They were then shaken in closed vials with about three times their bulk of ether, added in four successive portions and the etherial portion decanted and evaporated in contact with water acidulated with oxalic acid. The same bulks of etherial solution were obtained in each case, and the same amounts of the same strength of acidulated water used. The residues obtained were diluted to the same extent, and the farther dilution they would bear tested with the re-agent before mentioned. In this series of experiments, Squibb's fluid extract (of leaves) gave a

solution bearing dilution with 20 times its volume of water, Tilden's $1\frac{1}{2}$ times its volume, and Thayer's 4 times its volume, making the comparative strengths of Squibb's 42, Tilden's 5, and Thayer's 10.

Some fluid extract made from the fresh fruits of conium in 1854, in such a manner that a minim of the liquid represented a grain of the undried seeds, was also tested. The oxalic solution was found to bear dilution with 19 times its volume of water. If we suppose the seeds from which this preparation was made in 1854, to have been of equal strength with those gathered in 1866, it will follow that this preparation, after the lapse of 13 years, still retained about two-thirds of its original efficacy. But, of course, no reliable inferences can be drawn from a mere supposition.

The only experiment yet made by the writer, in the investigation in progress, to test the therapeutic effects of the conium, consisted in his swallowing 16 minims of Squibb's fluid extract of conium seed, with a view of arriving at some idea of the suitable medicinal dose. The quantity mentioned, taken about five hours after breakfast, produced marked operative effects in about twenty minutes. The effects manifested were a peculiar sensation of heaviness in the eyelids, and as it seemed some degree of ptosis, and a feeling akin to dizziness, that made it quite unpleasant to retain the sitting posture. There appeared to be no disposition to sleep produced. The effects were at their height in about an hour, and mainly passed away after the lapse of two hours from the time of taking the dose. A moderate meal had been eaten in the interval.

This experiment would indicate a suitable *commencing* dose of the fluid extract mentioned, to be about five minims.

What appears to have been arrived at by the experiments narrated is this: That the immature fruits of conium are far preferable to the leaves, that they may be dried without serious injury, and that a very active preparation may be made from them. The further course of this investigation, it is designed to direct toward ascertaining, if possible, some of the causes producing the want of uniformity and stability desirable in the preparations of Conium, with a view of obviating them, if it may be, and also toward obtaining such experimental knowledge of the physiological and therapeutic effects of the article in question as shall lead to additional practical applications of it.

Manlius, N. Y., *February* 4, 1867.